=> d his

(FILE 'HOME' ENTERED AT 10:22:28 ON 23 AUG 2000)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, SCISEARCH, BIOTECHDS' ENTERED AT 10:22:33 ON 23 AUG 2000

L1 266 S COMPUTER AND DATABASE AND CELL AND (LABEL OR DESCRIPTOR)
L2 37 S L1 AND IMAGE
L3 36 DUP REM L2 (1 DUPLICATE REMOVED)
L4 34 S L3 AND PY<2000

=> d ibib abs 14 1-5

L4 ANSWER 1 OF 34 MEDLINE
ACCESSION NUMBER: 1999131225 MEDLINE
DOCUMENT NUMBER: 99131225
TITLE: A web-accessible digital atlas of the distribution of nitric oxide synthase in the mouse brain.
AUTHOR: Cork R J; Perrone M L; Bridges D; Wandell J; Scheiner C A; Mize R R
CORPORATE SOURCE: Department of Cell Biology and Anatomy, Louisiana State University Medical Center, New Orleans 70112, USA.. jcork@lsumc.edu
CONTRACT NUMBER: EY-02973 (NEI)
NS36000 (NINDS)
SOURCE: PROGRESS IN BRAIN RESEARCH, **(1998)** 118 37-50.
Journal code: Q0B. ISSN: 0079-6123.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
ENTRY MONTH: 199906
ENTRY WEEK: 19990602
AB We have produced a digital atlas of the distribution of nitric oxide synthase (NOS) in the mouse brain as a reference source for our studies on the roles of nitric oxide in brain development and plasticity. NOS was labeled using nicotinamide adenine dinucleotide phosphate diaphorase (NADPHd) histochemistry. In addition, choline acetyltransferase (ChAT) immunocytochemistry was used to identify cholinergic **cells** because many of the NADPHd positive **cells** were thought to colocalize acetylcholine. Some sections were also labeled with antibodies to either the neuronal (nNOS) or endothelial (eNOS) isoforms of NOS. Series of sections from 11 C57/BL6 mice were collected and labeled for NADPHd and/or ChAT. We collected two types of data from this material: color digital photographs illustrating the density of **cell** and fiber labeling, and **computer**/microscope plots of the locations of all the labeled **cells** in selected sections. The data can be viewed as either a series of single-section maps produced by combining the plots with the digital **images**, or as 3-D views derived from the **cell** plots. The atlas of labeled **cell** maps, together with selected color photographs and 3-D views, is available for viewing via the World Wide Web (http:@nadph.anatomy.lsumc.edu). Examination of the atlas data has revealed several points about the distribution of NOS throughout the mouse brain. Firstly, different populations of NADPHd-positive neurons can be distinguished by different patterns of staining. In some brain areas neurons are intensely stained by the NADPHd

technique where **label** fills the **cell** bodies and much of the dendritic trees. In other brain regions labeling is much lighter, is principally confined to the cytoplasm of the cell soma, and extends only a short distance within proximal dendrites. Intense labeling is typical of neurons in the caudate/putamen and mesopontine tegmental nuclei. Most of the labeled neurons in the cortex also stain this way. Lighter, "granular" **label** is found in many other nuclei, including the medial septum, hippocampus, and cerebellum. In addition to staining pattern, we have also noted that different subpopulations of NOS-neurons can be distinguished on the basis of colocalization with ChAT.

Substantial overlap of the distributions of these two substances was observed although very little colocalization was found in most cholinergic **cell** groups except the mesopontine tegmental nuclei. Other points of interest arising from this project include the apparent lack of NADPHd labeling in the CA1 pyramidal **cells** of the hippocampus or the Purkinje neurons in the cerebellum. This observation is especially relevant given that synaptic plasticity in these regions is reported to be nitric-oxide dependent.

L4 ANSWER 2 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000:91531 BIOSIS
DOCUMENT NUMBER: PREV200000091531
TITLE: The microbial proteome **database**: An automated laboratory catalogue for monitoring protein expression in bacteria.
AUTHOR(S): Cordwell, Stuart J. (1); Nouwens, Amanda S.; Verrills, Nicole M.; McPherson, James C.; Hains, Peter G.; Van Dyk, Derek D.; Walsh, Bradley J.
CORPORATE SOURCE: (1) Australian Proteome Analysis Facility, Macquarie University, Level 4, Building F7B, Sydney, NSW, 2109 Australia
SOURCE: Electrophoresis, (**Dec.**, **1999**) Vol. 20, No. 18, pp. 3580-3588.
ISSN: 0173-0835.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Laboratories devoted to high-throughput characterisation of purified proteins arrayed via two-dimensional (2-D) gel electrophoresis face an arduous task in maintaining a centralised and constantly evolving record of information relating to the characterisation of proteins and their responses following biological challenges. The Microbial Proteome **Database** (MPD) has been conceived as an in-house resource for complementing the plethora of genomic **databases** available for such organisms. The **database** utilises commercially available software to provide an electronic 'lab book' of information obtained daily from 2-D electrophoresis gels, **image** analysis packages, protein characterisation methodologies, and biological experimentation. The MPD begins from a single 2-D gel **image** (a 2-D 'reference map') with clickable spots that link to a 'protein catalogue' (ProtCat) with spot information including protein identity, changes in expression determined under experimental conditions, cellular location, mass, and p/. The entry for each protein then contains further links to gel **images** corresponding to the presence of the particular protein within different subproteomes (as defined by the pH of narrow- and wide-range immobilised pH gradients or from differential extraction methods used to determine the location of the protein within a functional **cell**). The **database** currently contains information from strains of three microbial species (Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus) and 32 master gel **images**. The rapid accessibility of information obtained from microbial proteomes is an

essential step towards the integrated analysis of these organisms at the gene, transcript, protein and functional levels and will aid in reducing turnaround time between sample preparation and e discovery of molecules of biological significance.

L4 ANSWER 3 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000:91523 BIOSIS
DOCUMENT NUMBER: PREV200000091523
TITLE: Information transfer between large and small two-dimensional polyacrylamide gel electrophoresis.
AUTHOR(S): Felley-Bosco, Emanuela; Demalte, Isabelle; Barcelo, Silvia; Sanchez, Jean-Charles; Hochstrasser, Denis F.; Schlegel, Werner; Reymond, Marc A. (1)
CORPORATE SOURCE: (1) Klinik fuer Chirurgie, Otto-von-Guericke Universitaet Magdeburg, Leipziger Str. 44, 39120, Magdeburg Germany
SOURCE: Electrophoresis, (**Dec.**, **1999**) Vol. 20, No. 18, pp. 3508-3513.
ISSN: 0173-0835.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To determine the feasibility of data transfer, an interlaboratory comparison was conducted on colon carcinoma **cell** line (DLD-1) proteins resolved by two-dimensional polyacrylamide gel electrophoresis either on small (6 X 7 cm) or large (16X18 cm) gels. The gels were silver-stained and scanned by laser densitometry, and the **image** obtained was analyzed using Melanie software. The number of spots detected was 1337+-161 vs. 2382 +- 176 for small vs. large format gels, respectively. After gel calibration using landmarks determined using pI and Mr markers, large- and small-format gels were matched and 712+-36 proteins were found on both types of gels. Having performed accurate gel matching it was possible to acquire additional information after accessing a 2-D PAGE reference **database** (http://www.expasy.ch/cgibin/map2/ def?DLD1-HUMAN). Thus, the difference in gel size is not an obstacle for data transfer. This will facilitate exchanges between laboratories or consultation concerning existing **databases**.

L4 ANSWER 4 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:75549 BIOSIS
DOCUMENT NUMBER: PREV199900075549
TITLE: **Computer**-generated three-dimensional reconstructions of serially sectioned mouse embryos.
AUTHOR(S): Kaufman, M. H. (1); Brune, R. M.; Davidson, D. R.; Baldock, R. A.
CORPORATE SOURCE: (1) Dep. Anatomy, Univ. Med. Sch., Teviot Place, Edinburgh EH8 9AG UK
SOURCE: Journal of Anatomy, (**Oct.**, **1998**) Vol. 193, No. 3, pp. 323-336.
ISSN: 0021-8782.
DOCUMENT TYPE: General Review
LANGUAGE: English
AB We have been involved with a group of **computer** scientists and anatomists in the development of **computer**-based methodologies that not only combine the advantages of scanning electron microscopy and conventional histology, but provide the additional dimension of tissue recognition. The latter is achieved by the appropriate labelling of tissues and structures by delineation or 'painting'. Individually segmented anatomically defined tissues can be highlighted in a particular colour and viewed either in isolation or in combination with other appropriately labelled tissues and organs. Tissues can be shown in any orientation either as a transparent overlay on **computer**

-generated histological sections or as 3-D **images** without the histological background. An additional feature of the system is that **computer** graphics technology combined with 3-D glasses now also allows the viewer to see the object under analysis in stereo. This facility has been found to be particularly helpful in drawing attention to topological relationships that had not previously been readily noted. As the mouse is now the mammalian model of choice in many areas of developmental research, it is of critical importance that a basic level of skill is available in the research community in the interpretation of serially sectioned material, for example, for the rapidly expanding field in which gene expression studies play a significant role. It is equally important that there is an understanding of the dynamic changes that occur in relation to the differentiation of the various organ systems seen in these early stages of development. What we emphasize here is the additional information that it is possible to gain from the use of this tool which, in our view, could not readily have been gained from the analysis of scanning electron micrographs or by studying conventional serial histological sections of similar stages of mouse embryonic development. The methodology has been developed as part of a large project to prepare a **database** of mouse developmental anatomy covering all stages from fertilization to birth in order to allow the accurate spatial mapping of gene expression and **cell** lineage data onto the digital Atlas of normal mouse development. In this paper we show how this digital anatomical Atlas also represents a valuable teaching aid and research tool in anatomy.

L4 ANSWER 5 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:400315 BIOSIS
DOCUMENT NUMBER: PREV199800400315
TITLE: In vitro model system for the identification and characterization of proteins involved in inflammatory processes.
AUTHOR(S): Dax, Claudia I.; Lottspeich, Friedrich; Muellner, Stefan (1)
CORPORATE SOURCE: (1) Hoechst Res. and Technol. GmbH and Co. KG, G830, D-65926 Frankfurt Germany
SOURCE: Electrophoresis, (**July, 1998**) Vol. 19, No. 10, pp. 1841-1847.
ISSN: 0173-0835.
DOCUMENT TYPE: Article
LANGUAGE: English

AB An in vitro model featuring important inflammatory cellular states was established, based on the murine monocyte/macrophage **cell** line RAW 264.7. Macrophages are key players in chronic inflammation, and major parts of the biochemical reactions taking place in vivo, e.g., the production of proinflammatory cytokines, can be triggered in vitro by stimulation of the **cells** with bacterial lipopolysaccharide (LPS). A mastergel, representing a synthetic **image** of the expressed basic set of cellular proteins, was designed by a **computer**-assisted overlay of a statistically significant number of two-dimensional electrophoresis (2-DE) gels of unstimulated RAW 264.7 **cells**. This **image** served as a reference for qualitative and quantitative changes in the protein pattern induced by stimulation of the macrophages with LPS. The optimal conditions for LPS stimulation were evaluated by monitoring the expression and secretion of the proinflammatory cytokine tumor necrosis factor-alpha (TNF-alpha). The comparison of the mastergel with the 2-DE gels of LPS-stimulated **cells** revealed several changes in the protein pattern. In order to prove the relevance of the presented model system, we focused on two low molecular weight proteins, which showed significant changes in the apparent concentration in a 2-DE pattern. These proteins were further characterized by microsequencing of internal peptides. A comparison of the

obtained sequences with protein **databases** identified them as cofilin and keratinocyte lipid-binding protein.

=> d ibib abs l4 6-10

L4 ANSWER 6 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:312763 BIOSIS
DOCUMENT NUMBER: PREV199800312763
TITLE: Differentiation and characterization of enteroviruses by **computer**-assisted viral protein fingerprinting.
AUTHOR(S): Holland, Diane T. (1); Senne, Jill; Peter, C. R.; Urmeneta, Connie; Connor, J. D.
CORPORATE SOURCE: (1) Dep. Pediatr., 0808, Div. Infect. Dis., Univ. California, San Diego, 9500 Gillman Dr., La Jolla, CA 92093-0808 USA
SOURCE: Journal of Clinical Microbiology, (**June, 1998**) Vol. 36, No. 6, pp. 1588-1594.
ISSN: 0095-1137.
DOCUMENT TYPE: Article
LANGUAGE: English
AB We have developed and standardized a computerized method for the typing and characterization of enteroviruses with radiolabeled viral protein fingerprints. Enteroviral proteins were radiolabeled with (35S)methionine during growth in **cell** culture and were then separated by polyacrylamide gel electrophoresis. The dried gel was scanned, and from the resulting **computer image** (which resembled an autoradiogram) protein patterns were **computer** extracted and stored in a **database**. The enterovirus **database** contained community and prototype strains belonging to 20 different enteroviral serotypes. Each serotype has a discrete protein pattern, and the most important pattern differences for determining each type are in the region of the viral capsid proteins VP1, VP2, and VP3. When the **database** was challenged with 148 clinical enterovirus strains, 144 (97%) were correctly identified by using the correlation coefficient as a quantitative measure of relatedness between two patterns. This method can identify a type in a single test and represents a practical alternative to virus neutralization because it is less expensive, is much faster (3 rather than 10 days), and does not rely on any virus-specific reagents. The results also show that most of the strains currently isolated from the community have protein patterns different from those of their older prototype strains. Viral protein fingerprinting is an evolving, dynamic system for the typing and characterization of enteroviruses. The method is appropriate for use in clinical virology and reference laboratories for the typing of enteroviruses, for the study of the epidemiology of enteroviruses, and for surveillance of enteroviruses.

L4 ANSWER 7 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:223932 BIOSIS
DOCUMENT NUMBER: PREV199800223932
TITLE: An integrated approach to proteome analysis: Identification of proteins associated with cardiac hypertrophy.
AUTHOR(S): Arnott, David (1); O'Connell, Kathy L.; King, Kathleen L.; Stults, John T.
CORPORATE SOURCE: (1) Protein Chem. Dep., Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080 USA
SOURCE: Analytical Biochemistry, (**April 10, 1998**) Vol. 258, No. 1, pp. 1-18.
ISSN: 0003-2697.
DOCUMENT TYPE: Article

LANGUAGE: English

AB Hypertrophy of cardiac myocytes is a primary response of the heart to overload, and is an independent predictor of heart failure and death. Distinct cellular phenotypes are associated with hypertrophy resulting from different causes. These phenotypes have been described by others at the molecular level by analysis of gene transcription patterns. An alternative approach is the analysis of large-scale protein expression patterns (the proteome) by two-dimensional polyacrylamide gel electrophoresis. Realization of this goal requires the ability to rigorously analyze complex 2D gel **images**, efficiently digest individual gel isolated proteins (especially those expressed at low levels), and analyze the resulting peptides with high sensitivity for rapid **database** searches. We have undertaken to improve the technology and experimental approaches to these challenges in order to effectively study a **cell** culture model for cardiac hypertrophy. The 2D gel patterns for **cell** lysates from multiple samples of cardiac myocytes with or without phenylephrine-induced hypertrophy were analyzed and spots which changed in abundance with statistical significance were located. Eleven such spots were identified using improved procedures for in-gel digestion of silver-stained proteins and high-sensitivity mass spectrometry. The incorporation of low levels of sodium dodecyl sulfate into the digestion buffer improved peptide recovery. The combination of matrix-assisted laser desorption mass spectrometry for initial measurements and capillary liquid chromatography-ion trap mass spectrometry for peptide sequence determination yielded efficient protein identification. The integration of 2D gel **image** analysis and routine identification of proteins present in gels at the subpicomole level represents a general model for proteome studies relating genomic sequence with protein expression patterns.

L4 ANSWER 8 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:177426 BIOSIS
DOCUMENT NUMBER: PREV199800177426
TITLE: TMIG-2D PAGE: A new concept of two-dimensional gel protein **database** for research on aging.
AUTHOR(S): Toda, Tosifusa (1); Kaji, Kazuhiko; Kimura, Narimichi
CORPORATE SOURCE: (1) Dep. Molecular Biol., Tokyo Metropolitan Inst. Gerontology, 35-2 Sakaecho, Itabashiku, Tokyo 173 Japan
SOURCE: Electrophoresis, (**Feb.**, **1998**) Vol. 19, No. 2, pp. 344-348.
ISSN: 0173-0835.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Cellular proteins of a normal human diploid fibroblast line (TIG-3) at various stages of replicative aging were resolved by horizontal isoelectric focusing on an immobilized pH gradient, followed by vertical sodium dodecyl sulfate (SDS)-polyacrylamide gel electrophoresis (PAGE). Spot proteins were visualized by silver staining and quantitated by **image** processing. All corresponding spots were matched among two-dimensional gel **images**, and variation profiles in relative abundance of individual proteins during in vitro aging were classified into five categories, i.e., (i) increase, (ii) decrease, (iii) increase followed by decrease, (iv) decrease followed by increase, and (v) irregular or nonsignificant variation. The new concept of the Tokyo Metropolitan Institute of Gerontology two-dimensional gel protein **database** (TMIG-2DPAGE) was prepared from the above data to support research on cellular aging. The **database** was put on our World Wide Web home page at the URL of http://www.tmig.or.jp/2D/ to allow free access through the Internet. The individual protein data entries were linked to the standard spot protein map of the two-dimensional gel **image** in order to be accessible by clicking the mouse on it.

L4 ANSWER 9 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:53572 BIOSIS

DOCUMENT NUMBER: PREV199800053572
TITLE: High resolution urban morphology data for urban wind flow modeling.
AUTHOR(S): [redacted]onco, Ronald M. (1); Ellefsen, [redacted]chard
CORPORATE SOURCE: (1) US Army Res. Lab., Adelphi, MD 20783 USA
SOURCE: Atmospheric Environment, (**Jan.**, **1998**) Vol. 32, No. 1, pp. 7-17.
ISSN: 1352-2310.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The application of urban Forestry methods and technologies to a number of practical problems can be further enhanced by the use and incorporation of localized, high resolution wind and temperature fields into their analysis methods. The numerical simulation of these micrometeorological fields will represent the interactions and influences of urban structures, vegetation elements, and variable terrain as an integral part of the dynamics of an urban domain. Detailed information of the natural and man-made components that make up the urban area is needed to more realistically model meteorological fields in urban domains. Simulating high resolution wind and temperatures over and through an urban domain utilizing detailed morphology data can also define and quantify local areas where urban forestry applications can contribute to better solutions. Applications such as the benefits of planting trees for shade purposes can be considered, planned, and evaluated for their impact on conserving energy and cooling costs as well as the possible reconfiguration or removal of trees and other barriers for improved airflow ventilation and similar processes. To generate these fields, a wind model must be provided, as a minimum, the location, type, height, structural silhouette, and surface roughness of these components, in order to account for the presence and effects of these land morphology features upon the ambient airflow. The morphology of Sacramento, CA has been characterized and quantified in considerable detail primarily for wind Bow modeling, simulation, and analyses, but can also be used for improved meteorological analyses, urban forestry, urban planning, and other urban related activities. Morphology methods previously developed by Ellefsen are applied to the Sacramento scenario with a high resolution grid of 100 m X 100 m. The Urban Morphology Scheme defines Urban Terrain Zones (UTZ) according to how buildings and other urban elements are structured and placed with respect to each other. The urban elements within the 100m X 100 m **cells** (one hectare) are further described and digitized as building height, building footprint (in percent), reflectivity of its roof, pitched roof or flat, building's long axis orientation, footprint of impervious surface and its reflectivity, footprint or canopy elements, footprint of woodlots, footprint or grass area, and footprint of water surface. A variety of maps, satellite **images**, low level aerial photographs, and street level photographs are the raw data used to quantify these urban properties. The final digitized morphology **database** resides in a spreadsheet ready for use on ordinary personal **computers**.

L4 ANSWER 10 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1997:342141 BIOSIS
DOCUMENT NUMBER: PREV199799641344
TITLE: **Computer**-aided 3-D reconstruction of serially sectioned mouse embryos: Its use in integrating anatomical organization.
AUTHOR(S): Kaufman, M. H. (1); Brune, R. M.; Baldock, R. A.; Bard, J. B. L.; Davidson, D.
CORPORATE SOURCE: (1) Dep. Anatomy, Univ. Med. Sch., Teviot Place, Edinburgh EH8 9AG UK
SOURCE: International Journal of Developmental Biology, (1997) Vol.

41, No. 2, pp. 223-233.
ISSN: 0214-6282.
DOCUMENT TYPE: Article
LANGUAGE: English
AB This paper reviews recent work on a project that uses a **computer** -aided approach for making 3-D reconstructions of serially sectioned mouse embryos (the digital mouse). The captured **images** are aligned using a warping program so that almost perfect alignment of adjacent sections is achieved with minimal deformation. The sections that are viewed on the **computer** screen are in fact **computer** -generated grey-level **images** with a resolution of about 10 mu-m. The reconstructed embryo may then be resectioned in any plane to simulate as near as possible an exact match on the **computer** screen to the viewer's own material. Individual anatomical domains may then be painted in different colors, and these domains may be selected by querying the textual **database** containing anatomical and other information. Further, it is now possible to generate 3-D **images** of individual anatomically discrete components or related sets of components of a particular system in isolation from the rest of the embryo, or, if required, against a 'ghost-like' **image** of the intact embryo, or specific parts of an embryo. In the article examples are given of the use of the system in interpreting the vascular, gut and paraxial mesoderm systems, while both the advantages and disadvantages of this approach are also discussed. The eventual aim will be to provide 3-D reconstructions of mouse embryos from fertilization up to 14 days post coitum of development. When completed, this project will allow the accurate spatial mapping of gene-expression and **cell** lineage data onto the digital Atlas of normal mouse embryonic development.

=> d ibib abs l4 11-15

L4 ANSWER 11 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1997:290589 BIOSIS
DOCUMENT NUMBER: PREV199799589792
TITLE: Construction of HSC-2DPAGE: A two-dimensional gel electrophoresis **database** of heart proteins.
AUTHOR(S): Evans, Guy; Wheeler, Colin H.; Corbett, Joseph M.; Dunn, Michael J. (1)
CORPORATE SOURCE: (1) Division Cardiothoracic Surgery, Natl. Heart Lung Inst., Imperial Coll. Sch. Med., Heart Sci. Cent., Harefield Hosp., Middlesex UB9 6JH UK
SOURCE: Electrophoresis, (1997) Vol. 18, No. 3-4, pp. 471-479.
ISSN: 0173-0835.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The dissemination of information relating to the characterization of proteins from two-dimensional electrophoresis (2-DE) gel **databases** is essential for their effective utilization in the study of protein expression in **cell** biology. Since the inception of the World Wide Web and the pioneering development of SWISS-2DPAGE as a tool for retrieving information on proteins separated by 2-DE, the Internet has become the method of choice for disseminating and accessing information on 2-DE protein **databases**. At Harefield we have established HSC-2DPAGE which is an advanced interface for accessing protein **databases** relating to heart disease. The Web site currently includes **databases** of proteins from human, dog and rat ventricular tissue and a human endothelial **cell** line. The **databases** are searchable individually or as a whole by remote keyword searches. Each **database** is represented by both synthetic (**computer** generated) and real (scanned gel) clickable

images upon which characterized protein spots are highlighted by hyperlinked symbols. The **database** conforms to all the rules proposed for federated 2-DE protein **databases** and individual protein entries are linked to other protein **databases** such as SWISS-PROT by active cross-references. This paper describes the construction of HSC-2DPAGE, its maintenance, and access via the Internet.

L4 ANSWER 12 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1997:201129 BIOSIS
DOCUMENT NUMBER: PREV199799500332
TITLE: Standardization of protocol for Immobiline 2-D PAGE and construction of 2-D PAGE protein **database** on World Wide Web home page.
AUTHOR(S): Toda, Tosifusa (1); Kimura, Narimichi
CORPORATE SOURCE: (1) Dep. Mol. Biol., Tokyo Metropolitan Inst. Gerontol., 35-2 Sakae-cho, Itabashi-ku, Tokyo 173 Japan
SOURCE: Japanese Journal of Electrophoresis, (1997) Vol. 41, No. 1,
pp. 13-19.
ISSN: 0031-9082.
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
AB Organismic aging appears in the results of functional alteration of tissue-constituent **cells**. The replicative life span of normal human diploid fibroblasts in **cell** culture has been realized as a typical model of the research on mitotic **cell** aging. From the above premises, a new project has started in our institute for establishing my own age-related protein **database** of human diploid fibroblasts upon a 2-D PAGE technique. The protocol of 2-D PAGE with horizontal IPG-IEF and vertical SDS-PAGE was standardized including whole procedures from **cell** harvest through spot quantification, since the reproducibility of 2-D gel pattern depended on the procedure. The master 2-D gel pattern of human diploid fibroblasts was generated by merging skin fibroblast-specific spots into the standard 2-D gel pattern of lung fibroblasts in an **image** analyzing software, because fibroblasts showed tissue specificity. The master 2-D gel pattern with spot identification numbers and the **database** of age-dependent protein alteration were presented on my home page for free access through the Internet **computer** network.

L4 ANSWER 13 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1997:87462 BIOSIS
DOCUMENT NUMBER: PREV199799379175
TITLE: CDNA expression and human two-dimensional gel protein **databases**: Towards integrating DNA and protein information.
AUTHOR(S): Leffers, Henrik (1); Dejgaard, Kurt; Honore, Bent; Madsen, Peder; Nielsen, Morten S.; Celis, Julio E.
CORPORATE SOURCE: (1) Dep. Growth Reproduction, Sect. GR-5064, Rigshospitalet, Blegdamsvej, DK-2100 Copenhagen Denmark
SOURCE: Electrophoresis, (1996) Vol. 17, No. 11, pp. 1713-1719.
ISSN: 0173-0835.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The rapid progress in characterizing genes and mRNAs (expressed sequence tags, ESTs) as a result of the Human Genome Project makes it imperative to
develop strategies to interface DNA mapping and sequencing data with protein information, as the latter orchestrate most cellular functions. Presently, the only technique able to resolve and record the thousands of proteins present in **cells** and tissues is two-dimensional (2-D) gel electrophoresis in combination with **computer**-aided technology to scan the gels, make synthetic **images**, assign numbers to individual spots as well as to enter qualitative and quantitative information. To date, comprehensive 2-D gel **databases** containing information about various properties of proteins (cellular

localization, identification, regulatory properties, partial amino acid sequences, etc.) have been established (available on the internet: http://biobase.dk/cgi-bin/celis). What remains is to provide a link between these data and the forthcoming information from the Human Genome Project. We are pursuing two approaches to achieve this goal: (i) microsequencing and mass spectrometry analysis of proteins resolved from 2-D gels and (ii) expression of cDNAs in the vaccinia virus expression system. Using the latter approach we have expressed about 60 cDNAs in human **cells** under conditions that faithfully reproduce post-translational trimmings and modifications of the proteins. The method, in combination with 2-D gel electrophoresis, allows precise matching of almost any cDNA to its protein product, irrespective of the protein abundance.

L4 ANSWER 14 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1996:197031 BIOSIS
DOCUMENT NUMBER: PREV199698753160
TITLE: A model-based approach for determining orientations of biological macromolecules imaged by cryoelectron microscopy.
AUTHOR(S): Baker, Timothy S. (1); Cheng, R. Holland
CORPORATE SOURCE: (1) Dep. Biol. Sci., Purdue Univ., West Lafayette, IN 47907-1392 USA
SOURCE: Journal of Structural Biology, (1996) Vol. 116, No. 1, pp. 120-130.
ISSN: 1047-8477.
DOCUMENT TYPE: Article
LANGUAGE: English
AB A polar Fourier transform (PFT) method is described that facilitates determination and refinement of orientations of individual biological macromolecules imaged with cryoelectron microscopy techniques. A three-dimensional density map serves as a high signal-to-noise model from which a PFT **database** of different views is generated and against which the PFTs of individual **images** are correlated. The PFT produces rotation-invariant data particularly well-suited for rapid and accurate determination of orientation parameters. The method relies on accurate knowledge of the center of symmetry and radial scale of both model and **image** data but is insensitive to the relative contrast and background values of these data. Density maps may be derived from a variety of sources such as **computer**-generated models, X-ray crystallographic structures, and three-dimensional reconstructions computed from **images**. The PFT technique has been particularly useful for the analysis of particles with icosahedral symmetry and could be adapted for the analysis of single particles of any symmetry for which a crude model exists or can be produced.

L4 ANSWER 15 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1996:189776 BIOSIS
DOCUMENT NUMBER: PREV199698745905
TITLE: Sterecon: Three-dimensional reconstructions from stereoscopic contouring.
AUTHOR(S): Marko, Michael; Leith, Ardean
CORPORATE SOURCE: Biol. Microscopy Image Reconstruction Resource, Wadsworth Center, New York State Dep. Health, P.O. Box 509, Empire State Plaza, Albany, NY 12201-0509 USA
SOURCE: Journal of Structural Biology, (1996) Vol. 116, No. 1, pp. 93-98.
ISSN: 1047-8477.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Sterecon is a system for making 3-D reconstructions or measurements by tracing from stereopair **images**. The stereopair **images** may come directly from a microscope, such as a transmission or scanning electron microscope. Alternatively, the **images** may be created from a stack of thin slices, such as a confocal light microscopy depth series, an electron tomographic volume, or a set of serial histological

slices. When the structure to be studied is thick or complex, a serial stack of stereoscopic **images** can be used. Objects are traced within the **images**, and their coordinates are entered into a line or contour **database**. The contour **database** can be used for 3-D structure measurement, and the contours can be displayed as a reconstruction. Sterecon has interfaces from other software which can generate the input **images** and to other software for further display and analysis.

=> d ibib abs l4 16-20

L4 ANSWER 16 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1996:31059 BIOSIS
DOCUMENT NUMBER: PREV199698603194
TITLE: The evaluation and implementation of match criteria for forensic analysis of DNA.
AUTHOR(S): Laber, Terry L. (1); Iverson, James T.; Liberty, James A.; Giese, Staci A.
CORPORATE SOURCE: (1) Minn. Forensic Sci. Lab., Biol. Sect., 1246 University Ave., St. Paul, MN 55104 USA
SOURCE: Journal of Forensic Sciences, (1995) Vol. 40, No. 6, pp. 1058-1064.
ISSN: 0022-1198.
DOCUMENT TYPE: Article
LANGUAGE: English
AB This study describes a method for establishing match criteria used in forensic DNA typing. The validity of applying different match criteria based upon the molecular weight of a DNA band is discussed. The match criteria presented allow visually matching DNA patterns to be confirmed by **computer** assisted **image** analysis over the entire range of the sizing ladder. Approximately 5000 intragel and 5000 intergel comparisons were made between the restriction fragment length polymorphism (RFLP) DNA band sizes obtained from casework, mock cases, and environmentally insulted samples and the band sizes obtained from their corresponding bloodstain standards (controls). Analyses of these data suggested that fragments located in different molecular weight size regions of an analytical gel required different match criteria for assessing a visual match. The results of these analyses support the use of the following match criteria: Intragel 0.5-10 kb = +-1.7%, 10-15 kb = +-3.2%, 15-22.6 kb = +-5.8%; Intergel and blind control 0.5-10 kb = +-3.0%, 10-15 kb = +-4.2%, 15-22.6 kb = +- 10.0%; and human **cell** -line K562 and the monomorphic locus D7Z2 = +-2.5%. Each match criterion was also evaluated with respect to the distance in millimeters between matching bands throughout the 0.5-22.6 kb molecular weight size range. Applying these match criteria to different gel regions has been shown to be valid and reliable in comparisons conducted on more than 10,000 validation samples, in over 500 forensic cases and in more than 200 searches of a criminal sexual offender (CSO) **database** containing over 5000 individuals.

L4 ANSWER 17 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1996:25399 BIOSIS
DOCUMENT NUMBER: PREV199698597534
TITLE: A method for 3D reconstruction of neuronal processes using semithin serial sections displayed as a cinematographic sequence.
AUTHOR(S): Skoglund, T. S. (1); Pascher, R.; Berthold, C.-H.
CORPORATE SOURCE: (1) Dep. Anatomy Cell Biol., Univ. Goteborg, Medicinaregatan 3, S-413 90 Goteborg Germany
SOURCE: Journal of Neuroscience Methods, (1995) Vol. 61, No. 1-2, pp. 105-111.

ISSN: 0165-0270.
DOCUMENT TYPE: Article
LANGUAGE: English
AB In order to study the organization and distribution of dendrites and axons
in the cerebral cortex, we have developed a **computer**-assisted method for 3D reconstruction of neuronal processes based on serial light microscopic **images** displayed as a continuous sequence. A series of tangential sections (0.65 mu-m thick) through rat parietal cortex was aligned, digitized into the **computer** and then used to build a sequence (stack) of **images** which was stored to a digital real-time video disk. Apical dendrites located in dendritic bundles in laminae III and IV were traced through the sequence. Two tracing modes were tested: (1) cinematographic mode, in which the **image** stack was displayed continuously and automatically by the **computer** at various preset speeds (max. speed: 25 **images**/s) and (2) stepping mode, in which the interval between each **image** was varied manually according to the choice of the operator. Coordinates were stored in a **database** and used to build a 3D reconstruction where apical dendrites were displayed as wires or tubes. Tracing in cinematographic mode was about 3 times faster than tracing in stepping mode. We believe that the former mode exploits the built in 'filtering' capacity of the visual system to perform temporal averaging.

L4 ANSWER 18 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1995:77761 BIOSIS
DOCUMENT NUMBER: PREV199598092061
TITLE: The effect of reducing the number of **cells** scored on the performance of the in vivo rat liver UDS assay.
AUTHOR(S): Kennelly, J. C. (1); Pate, I.; Greenwood, M. R.
CORPORATE SOURCE: (1) Zeneca Pharmaceuticals, Alderley Park, Macclesfield SK10 4TG UK
SOURCE: Mutation Research, (1995) Vol. 334, No. 1, pp. 91-96. ISSN: 0027-5107.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The most labour-intensive feature of the in vivo rat liver UDS assay is the scoring of hepatocyte autoradiograms by microscope. Even with **image** analyser and **computer** equipment the scoring phase of a full study might require half of the technical effort applied. Practice recommended by guidelines has been to score 50 **cells** /slide and two slides per animal. Now sufficient data have been accumulated, an evaluation was made to observe whether this procedure was necessary. An analysis of the accumulated UDS **database** in our laboratory was made to determine the sources of variability of mean net nuclear grain count, (N - C). It was observed that the two largest components of variation in negative control animal mean (N - C) were between-day and interanimal variability. The contribution from sampling error during slide scoring was relatively small. Theoretical calculations showed that the greater sampling error derived from scoring 30 rather than
50 **cells**/slide would result in only a marginal increase in total assay variation. To test this, 30 **cells**/slide were randomly selected from the 50 **cells** scored originally in negative control animals in each of 18 studies over an 18-month period. It was confirmed that reducing the number of **cells** had a negligible effect on the variation of negative control animal mean (N - C) values. Furthermore, analysis of data from 10 more studies confirmed that within-study variation would be essentially unaffected by scoring 30 **cells** /slide. The use of 30 rather than 50 **cells** per slide (a total of 60 **cells** per animal) has therefore been adopted for all current studies and scoring procedures modified to avoid operator bias during the selection of a smaller number of **cells**.

L4 ANSWER 19 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1995:19389 BIOSIS

DOCUMENT NUMBER: PREV199598033689
TITLE: Secretagogue regulation of pancreatic acinar **cell** protein phosphorylation shown by rge-scale 2D-PAGE.
AUTHOR(S): [redacted]shart, Matthew J. (1); Groblew , Guy; Goke, Burkhard J.; Wagner, Andreas C. C.; Williams, John A.
CORPORATE SOURCE: (1) 7744 Med. Sci. II, Dep. Physiol., Univ Michigan, Ann Arbor, MI 48109-0622 USA
SOURCE: American Journal of Physiology, (1994) Vol. 267, No. 4 PART 1, pp. G676-G686.
ISSN: 0002-9513.
DOCUMENT TYPE: Article
LANGUAGE: English

AB High-resolution large-scale two-dimensional polyacrylamide gel electrophoresis (2D-PAGE) combined with **computer**-assisted **image** analysis was used to construct a **database** of secretagogue/second messenger-induced phosphoprotein modifications in intact rat pancreatic acinar **cells**. Isolated acini were labeled with 32P-i, exposed to hormones and other test agents, and subjected to large-scale 2D-PAGE and autoradiography. This procedure resolved 500 phosphoproteins in pancreatic acinar whole **cell** lysates. apprx 90% of which were localized in the soluble fraction of centrifuged samples. Soluble proteins were further characterized as to heat and acid stability. Cholecystokinin (CCK), carbachol, and bombesin altered the phosphorylation state of about 27 proteins with both increases and decreases observed. Subsets of proteins were phosphorylated in response to phorbol ester 12-O-tetradecanoylphorbol 13-acetate (TPA), calcium ionophore A-23187, and adenosine 3',5'-cyclic monophosphate (cAMP) analogue 8-bromo-cAMP. One of these proteins was identified as the myristoylated, alanine-rich, C-kinase substrate (MARCKS) protein by immunoprecipitation. The time course and dose response of phosphorylation changes due to CCK showed considerable variation between proteins, although a temporal hierarchy of phosphorylation events was clearly exhibited. Particularly striking was the rapid dephosphorylation within 30 s of a 19-kDa soluble protein to a minimum of 20 +- 1% of control. Increased phosphorylation of the MARCKS and other TPA-regulated proteins suggests that CCK, carbachol, bombesin, and the CCK partial agonist, JMV-180, all activate protein kinase C in intact acini.

L4 ANSWER 20 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1994:501835 BIOSIS
DOCUMENT NUMBER: PREV199497514835
TITLE: Pattern interpretation by cellular automata (PICA) - Evaluation of tumour **cell** adhesion in human melanomas.
AUTHOR(S): Smolle, Josef (1); Hofmann-Wellenhof, Rainer; Kerl, Helmut
CORPORATE SOURCE: (1) Dep. Dermatol., Analytical Morphol.-Tumor Biol. Div., Auenbruggerpl. 8, A-8036 Graz Austria
SOURCE: Analytical Cellular Pathology, (1994) Vol. 7, No. 2, pp. 91-106.
ISSN: 0921-8912.
DOCUMENT TYPE: Article
LANGUAGE: English

AB In routine pathology, the evaluation of the pattern of a tumour at scanning magnification often reveals diagnostic and prognostic features indicating that the biological properties of the tumour **cells** are related to the morphological pattern. For further evaluation of the relationship between functional properties of the **cells** on the one hand and the pattern on the other, we propose the pattern interpretation by cellular automata (PICA) procedure. The PICA system consists of an import module transferring real histological **images** into the data structure of a cellular automaton, a measurement module generating a comparable quantitative description of real and simulated **images**, a cellular automaton designed to simulate tumour growth

and invasion at the histological level, a **database** consisting of the morphological results obtained in simulated patterns, an interpretation module linking real histological **images** to the knowledge stored in the **database** and an **image** synthesis and display module. By comparing real **images** to **computer**-simulated patterns, PICA facilitates an estimation of functional properties based on the static histological pattern of a given tumour. Using the example of tumour **cell** adhesion, it is demonstrated that the degrees of tumour-tumour and tumour stroma adhesion significantly affect the resulting simulated patterns, that, in turn, the morphological evaluation of the patterns enables a reproducible estimation of adhesion and that estimates of adhesion in real **images** of malignant melanoma of the skin are of prognostic significance. PICA may serve as an additional in situ evaluation technique linking morphological features to functional properties.

=> d ibib abs l4 21-25

L4 ANSWER 21 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1994:372255 BIOSIS
DOCUMENT NUMBER: PREV199497385255
TITLE: A system for improved knowledge acquisition and understanding of results in **image** cyto- and histometry.
AUTHOR(S): Datta, A.
CORPORATE SOURCE: CSSC, Indian Statistical Inst., Calcutta India
SOURCE: Analytical Cellular Pathology, (1994) Vol. 6, No. 3, pp. 236.
Meeting Info.: Third Conference of the European Society for Analytical Cellular Pathology Grenoble, France May 16-20, 1994
ISSN: 0921-8912.
DOCUMENT TYPE: Conference
LANGUAGE: English

L4 ANSWER 22 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1994:342916 BIOSIS
DOCUMENT NUMBER: PREV199497355916
TITLE: Measuring activation patterns of the heart at a microscopic size scale with thin-film sensors.
AUTHOR(S): Hofer, Ernst (1); Urban, Gerald; Spach, Madison S.; Schafferhofer, Ingrid; Mohr, Gunther; Platzer, Dieter
CORPORATE SOURCE: (1) Inst. Med. Physik Biophysik, Karl-Franzens-Univ. A-8010 Graz Austria
SOURCE: American Journal of Physiology, (1994) Vol. 266, No. 5 PART 2, pp. H2136-H2145.
ISSN: 0002-9513.
DOCUMENT TYPE: Article
LANGUAGE: English
AB To study the spread of excitation in ventricular heart preparations we have designed a fast, high-resolution recording and mapping system. Papillary muscles were dissected from the isolated guinea pig hearts. The preparation was fixed in a tissue bath and superfused with Tyrode solution. Linear and two-dimensional arrays of Ag/AgCl electrodes were made on glass with a thin-film technique. The transparent sensors with up to 24 electrodes (spaced 50, 90, or 180 mu-m apart) were positioned close to the surface of the preparation with a custom-designed three-dimensional micromanipulator. Extracellular signals were simultaneously recorded by a

24-channel data acquisition system with a 200 kHz per channel sample rate, with 12-bit amplitude resolution and a maximum data length of up to 3 MB. Digitized video **images** of the electrode array and the underlaying preparation were used to identify the locations of the recording sites. A UNIX-based **computer** system with a custom-designed data acquisition and **database** program was used to control the instruments and to manage the experimental data. This technique gave signals with excellent signal-to-noise ratios (up to 65 dB) and permitted accurate evaluation of the time and the site of the local activation with high resolution (to within 5 ps, 50 mu-m). We describe the spread of excitation within the area of a few **cells** and found a substantial dispersion of conduction velocities. Beat-to-beat comparison of activation patterns showed relatively small variations in the spread of excitation (a few microseconds).

L4 ANSWER 23 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1994:270752 BIOSIS
DOCUMENT NUMBER: PREV199497283752
TITLE: Classification of chromosomes using a probabilistic neural network.
AUTHOR(S): Sweeney, Walter P., Jr.; Musavi, Mohamed T. (1); Guidi, John N.
CORPORATE SOURCE: (1) Univ. Maine, Dep. Electrical Computer Eng., Orono, ME 04469-5708 USA
SOURCE: Cytometry, (1994) Vol. 16, No. 1, pp. 17-24.
ISSN: 0196-4763.
DOCUMENT TYPE: Article
LANGUAGE: English
AB This paper describes the application of a probabilistic neural network (PNN) to the classification of normal human chromosomes. The inputs to the network are 30 different features extracted from each chromosome in digitized **images** of metaphase spreads. The output is 1 of 24 different classes of chromosomes (the 22 autosomes plus the sex chromosomes X and Y). An updating procedure was implemented to take advantage of the fact that in a normal somatic **cell** only two chromosomes can be assigned to each class. The network has been tested using the Copenhagen, Edinburgh, and Philadelphia **databases** of digitized **images** of human chromosomes. The recognition rates achieved in this study are superior to those reported using either the maximum likelihood or back propagation neural network techniques.

L4 ANSWER 24 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1994:209149 BIOSIS
DOCUMENT NUMBER: PREV199497222149
TITLE: Insulin family growth factors have specific effects on protein synthesis in preimplantation mouse embryos.
AUTHOR(S): Shi, C. Z.; Collins, H. W.; Buettger, C. W.; Garside, W. T.; Matschinsky, F. M.; Heyner, S. (1)
CORPORATE SOURCE: (1) Dep. Obstet. Gynecol., Univ. Pa. Med. Cent., 311A Jules Morgan Build., 36th and Hamilton Walk, Philadelphia, PA 19104-6080 USA
SOURCE: Molecular Reproduction and Development, (1994) Vol. 37, No. 4, pp. 398-406.
ISSN: 1040-452X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Previously constructed protein **databases** for two stages of preimplantation mouse embryogenesis, the compacted eight-**cell** stage and the fully expanded blastocyst stage, have been used to analyze

the effects of insulin, IGF-I, and IGF-II on protein synthesis in these developmental stages. Proteins were labeled by placing, for 2 hr, synchronous cohorts of 35-50 embryos into human tubal fluid (HTF) medium containing L-(35S)methionine (1 mCi/ml) in the presence or absence of one of the growth factors. The embryos were then washed with medium and lysed.

Samples were processed for 2-D gel analysis. For each embryonic stage and each growth factor, four or five experimental replicates were done and the gel **images** were compared using the PDQUEST system. Using the **computer**-assisted analysis, we were able to identify proteins that showed a statistically significant (P lt 0.05) change in synthesis. At the eight-**cell** stage of development insulin caused increased synthesis of two proteins and decreased synthesis in three proteins. Insulintreated blastocyst stage embryos exhibited an increased synthesis in eight proteins and decreased synthesis for one protein. The effect of IGF-I at the eight-**cell** stage of development was mostly inhibitory; the synthesis of only one protein increased and the synthesis of five proteins showed a decrease. Similar results were obtained with blastocyst stage embryos; four proteins demonstrated an increase in synthesis while 14 proteins showed a decrease. Eight-**cell** stage embryos incubated with IGF-II had seven proteins with a decreased synthesis, although in blastocyst stage embryos, nine proteins showed increased synthesis. However, seven IGF response proteins were found to be proteins that showed significant changes in isotope incorporation during the eight-**cell** to blastocyst stage of development (Shi et al., 1993). In all, 54 proteins were affected, and these were unique; thus, protein synthesis in preimplantation mouse embryos is influenced by insulin and the IGF-s, and further, each growth factor affects specific proteins.

L4 ANSWER 25 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1994:73765 BIOSIS
DOCUMENT NUMBER: PREV199497086765
TITLE: Protein **databases** for compacted eight-**cell** and blastocyst-stage mouse embryos.
AUTHOR(S): Shi, C. Z.; Collins, H. W.; Garside, W. T.; Buettger, C. W.; Matschinsky, F. M.; Heyner, Susan (1)
CORPORATE SOURCE: (1) Div. Reproductive Biology, Dep. Obstetrics Gynecology, 311A John Morgan Building, 36th and Hamilton Walk, Philadelphia, PA 19104-6080 USA
SOURCE: Molecular Reproduction and Development, (1994) Vol. 37, No. 1, pp. 34-47.
ISSN: 1040-452X.
DOCUMENT TYPE: Article
LANGUAGE: English

AB High-resolution two-dimensional sodium dodecyl sulfate-polyacrylamide (2D-SDS) gel electrophoresis combined with computerized analysis of gel **images** was used to construct and analyze protein **databases** for two stages of preimplantation mouse embryogenesis, the compacted eight-**cell** stage and the fully expanded blastocyst stage. These stages were chosen for their ease in identification of multiple synchronous embryos. Synchronous cohorts of 30-50 embryos were labelled with L-(35S)methionine for 2 hr. The embryos were then lysed in 30 mu-l hot SDS sample buffer, and the lysates were stored at -80 degree C until the gels were run. Five replicates were run for eight-**cell** embryos, and four for blastocyst-stage embryos. The samples were processed for 2D gel electrophoresis and fluorography; multiple exposures were made.

Gel **images** were analyzed using the PDQUEST system, and **databases** were constructed. Analysis of the **databases** for both developmental stages showed high reproducibility of protein spots

in multiple gel **images**. Of 1,674 total spots in eight-**cell** embryo standards, gt 79% of spots had a percentage error (S.E.M./averag lt 50%, and gt 45% had a percentage error lt 30%. Similarly, of 53 total spots in blastocyst-stage embryo standards, 74% of spots had a percentage error lt 50%, and approximately 47% of spots had a percentage error lt 30%. Forty-three spots (approximately 3% of the total spots) were found to be detected only in the eight-**cell** stage, while 75 spots were detected solely in the blastocyst stage. Sixty-nine proteins showed a greater than threefold increase in isotope incorporation from the eight-**cell** to the blastocyst stage, with a percentage error lt 50% in both the eight-**cell** and the blastocyst stages. In contrast, 41 of the proteins showed a decrease during this period. Analysis of the protein **databases** described in this study has allowed us to document the overall quantitative changes in proteins from the compacted eight-**cell** stage to the blastocyst stage of mouse preimplantation development. These **databases** provide a valuable tool for further detailed quantitative analysis of specific proteins associated with developmental events. In addition they will permit analysis of the effects of environmental factors, such as growth factors, on early embryo development.

=> d ibib abs l4 26-30

L4 ANSWER 26 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1994:47035 BIOSIS
DOCUMENT NUMBER: PREV199497060035
TITLE: Chromosome 3 **image database**: A program for **image** and text retrieval for chromosome mapping and the verification of probe tagged sites.
AUTHOR(S): Scott, Pat; Drabkin, Harry; Gemmill, Robert
CORPORATE SOURCE: Eleanor Roosevelt Inst., Univ. Colo. Health Sciences Cent., CO USA
SOURCE: Cytogenetics and Cell Genetics, (1994) Vol. 65, No. 1-2, pp. 45-46.
Meeting Info.: Fourth International Workshop on Human Chromosome 3 Mapping 1993 Groningen, Netherlands May 14-15, 1993
ISSN: 0301-0171.
DOCUMENT TYPE: Conference
LANGUAGE: English

L4 ANSWER 27 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1993:399193 BIOSIS
DOCUMENT NUMBER: PREV199345058018
TITLE: CUCUMIS.
AUTHOR(S): Kirkbride, Joseph H. Jr.
CORPORATE SOURCE: U.S. Dep. Agric., Agric. Res. Serv., Syst. Bot. Mycol. Lab., Room 304, Build. 011A, BARC-West, 10300 Baltimore Blvd., Beltsville, MD 20705-2350 USA
SOURCE: Kirkbride, J. H., Jr.. (1993) pp. No pagination. CUCUMIS. Publisher: Parkway Publishers Box 3678, Boone, North Carolina, USA.
DOCUMENT TYPE: Book
LANGUAGE: English
AB SPECIFICATIONS: IBM or compatible microcomputer. 1.2M floppy drive. Hard drive. VGA graphics card required for graphic **images**. Manuals and documentation on disk. One 5.25 inch floppy disk included. DESCRIPTION: This software is included with "Biosystematic Monograph of the Genus Cucumis (Cucurbitaceae)", by Joseph H. Kirkbride, Jr., Parkway Publishers, 1993 (reviewed separately). The morphological, cytological,

and macrodistributional data contained in the monograph are included in DELTA format for interactive specimen identification and for data querying. The files contained on the disk are: CUDIST.EXE, a self-extracting CUCUMIS collections **database** (2M) CUCUMIS.DOC, ASCII documentation for using the CUCUMIS **databases**; CUCUMIS.EXE, a self-extracting CUCUMIS morphological, cytological, and distributional **database** without graphic **images** (0.2M), for use with INTKEY; **IMAGES**.EXE, a self-extracting CUCUMIS morphological, cytological, and distributional **database** with graphic **images** (0.3M), for use with INTKEY; INTKEY.DOC, documentation for INTKEY; INTKEY30.EXE, self-extracting INTKEY, version 3.03, and its documentation (0.4M); LIST.COM, shareware program for browsing ASCII text files, version 7.5b; LIST.DOC, documentation for LIST.COM; README.1ST, disk documentation; SL.COM, shareware ASCII text editor; and SLED.DOC, documentation for SL.COM. INTKEY is an interactive program for accessing descriptive data, stored in DELTA format, of taxa. It can be used to identify unknown specimens or query data associated with taxa. INTKEY is menu driven or run from a command line and is user friendly with HELP functions readily available.

L4 ANSWER 28 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1992:305498 BIOSIS
DOCUMENT NUMBER: BA94:18648
TITLE: A COMPUTERIZED SYSTEM FOR MEASURING **CELL** LENGTH OF SINGLE ISOLATED SMOOTH MUSCLE **CELLS**.
AUTHOR(S): MOUMMI C; WOODFORD M
CORPORATE SOURCE: DIV. GASTROINTESTINAL DISEASES RES., SEARLE RES. AND DEV., 4901 SEARLE PARKWAY, SKOKIE, ILL. 60077.
SOURCE: DRUG DEV RES, (1992) 25 (4), 325-329.
CODEN: DDREDK. ISSN: 0272-4391.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB We have developed a state-of-the-art computerized system to measure the **cell** length (contraction/relaxation) of single isolated gastrointestinal smooth muscle **cells** in response to different drugs. The system is composed of a microscope to which a video camera is attached and a video monitor which is connected to the video camera output. The **image** on the TC screen is analyzed by a digital **image** processor. The data acquisition and initial analysis are done directly on a personal **computer**. The acquired data are sent immediately via a network to a **database** on a minicomputer. From this **database**, comprehensive data reports and graphs can be generated and hard copy obtained. The system was validated by testing the contractile activity of endothelin-1 and the relaxant effect of isoproterenol on single smooth muscle **cells** isolated from the rat colon. This system offers a valuable pharmacological tool for drug screening to the pharmaceutical industry.

L4 ANSWER 29 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1991:182868 BIOSIS
DOCUMENT NUMBER: BA91:97617
TITLE: THE MRC-5 HUMAN EMBRYONAL LUNG FIBROBLAST TWO-DIMENSIONAL GEL CELLULAR PROTEIN **DATABASE** QUANTITATIVE IDENTIFICATION OF POLYPEPTIDES WHOSE RELATIVE ABUNDANCE DIFFERS BETWEEN QUIESCENT PROLIFERATING AND SV-40 TRANSFORMED **CELLS**.
AUTHOR(S): CELIS J E; DEJGAARD K; MADSEN P; LEFFERS H; GESSER B; HONORE B; RASMUSSEN H H; OLSEN E; LAURIDSEN J B; ET AL
CORPORATE SOURCE: INST. MED. BIOCHEM. AND BIOREGULATION RES. CENTRE, OLE WORMS ALLE, BUILD. 170, UNIVERSITY PARK, DK-8000 AARHUS C, DENMARK.
SOURCE: ELECTROPHORESIS, (1990) 11 (12), 1072-1113.
CODEN: ELCTDN. ISSN: 0173-0835.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB A new version of the MRC-5 two-dimensional gel cellular protein **database** (Celis et al., Electrophoresis 1989, 10, 76-115) is presented. Gels were scanned with a Molecular Dynamics laser scanner and processed by the PDQUEST IITM software. A total of 1985 [35S]methionine-labeled cellular polypeptides (1323 with isoelectric focusing and 572 with nonequilibrium pH gradient electrophoresis) are recorded in this **database**, containing quantitative and qualitative data on the relative abundance of cellular proteins synthesized by quiescent, proliferating and SV40 transformed MRC-5 fibroblasts. Of the 592 proteins quantitated so far, the levels of 138 were up- or down-regulated (51 and 87, respectively) by two times or more in the transformed **cells** as compared to their normal proliferating counterparts, while only 14 behaved similarly in quiescent **cells**. Seven MRC-5 SV40 proteins, including plastin and two interferon-induced proteins, were not detected in the master MRC-5 **images**. The identity of 36 of the transformation-sensitive proteins whose levels are up or down regulated by two times or more was determined and additional information can be transferred from the master transformed human epithelial amnion **cells** (AMA) **database** (Celis et al., Electrophoresis 1990, 11,989-1071) for those polypeptides of known and unknown identity that have been matched to AMA polypeptides. As more information is gathered in this and other laboratories, including data on oncogene proteins and transcription factors, this comprehensive **database** will outline an integrated picture of the expression levels and properties of the thousands of protein components of organelles, pathways and cytoskeletal systems that may be directly or indirectly involved in properties associated with the transformed state.

L4 ANSWER 30 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1991:29323 BIOSIS
DOCUMENT NUMBER: BA91:18674
TITLE: CESAR A **COMPUTER** SUPPORTED MEASUREMENT SYSTEM FOR THE ENHANCEMENT OF DIAGNOSTICS AND QUALITY IN CYTOLOGY.
AUTHOR(S): GAHM T; AEIKENS B
CORPORATE SOURCE: INST. FUER THEORETISCHE NACHRICHTENTECHNIK UND INFORMATIONSVERARBEITUNG, UNIV. HANNOVER, FRG.
SOURCE: MICRON MICROSC ACTA, (1990) 21 (1-2), 29-56.
CODEN: MMACDN. ISSN: 0739-6260.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB In the following presentation, the concept of the CESAR Cytology system (**CEll** Screen and Analysing Routine system) is introduced, which unlike conventional systems also comprehensively integrates human empiric knowledge in the evaluation and interpretation of the measurement results.
For this purpose CESAR is especially equipped with an object-oriented data
base. Due to its special structure graphical presentations of the measurement or classification results (histograms, scatterplots) can be used as directories of a **cell image** data base. In this way the numerical results can be 'translated' into **cell images** with a similar content of information, but which are far better suited to be compared with the empirical knowledge of the human brain.

=> d ibib abs l4 31-34

L4 ANSWER 31 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1990:491481 BIOSIS
DOCUMENT NUMBER: BA90:119827
TITLE: STRUCTURE-BASED DESIGN OF NONPEPTIDE INHIBITORS SPECIFIC FOR THE HUMAN IMMUNODEFICIENCY VIRUS 1 PROTEASE.
AUTHOR(S): DESJARLAIS R L; SEIBEL G L; KUNTZ I D; FURTH P S; ALVAREZ J

C; ORTIZ DE MONTELLANO P R; DECAMP D L; BABE L M; CRAIK C S
CORPORATE SOURCE: DEP. PHARMACEUTICAL CHEM., SCH. PHARM., UNIV. CALIF., SAN FRANCISCO, CALIF. 94143-0446.
SOURCE: PROC NATL ACAD SCI U S A, (1990) 87 (17), 6644-6648. CODEN: PNASA6. ISSN: 0027-8424.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB By using a structure-based **computer**-assisted search, we have found a butyrophenone derivative that is a selective inhibitor of the human immunodeficiency virus 1 (HIV-1) protease. The **computer** program creates a negative **image** of the active site cavity using the crystal structure of the HIV-1 protease. This **image** was compared for steric complementarity with 10,000 molecules of the Cambridge Crystallographic **Database**. One of the most interesting candidates identified was bromperidol. Haloperidol, a closely related compound and known antipsychotic agnet, was chosen for testing. Haloperidol inhibits the HIV-1 and HIV-2 proteases in a concentration-dependent fashion with a Ki of .apprxeq. 100 .mu.M. It is highly selective, having little inhibitory effect on pepsin activity and no effect on renin at concentrations as high as 5 mM. The hydroxy derivative of haloperidol has a similar effect on HIV-1 protease but a lower potency against the HIV-2 enzyme. Both haloperidol and its hydroxy derivative showed activity against maturation of viral polypeptides in a **cell** assay system. Although this discovery holds promise for the generation of nonpeptide protease inhibitors, we caution that the serum concentrations of haloperidol in normal use as an antipsychotic agent are < 10 ng/ml (0.03 .mu.M). Thus, concentrations required to inhibit the HIV-1 protease are > 1000 times higher than the concentrations normally used. Haloperidol is highly toxic at elevated does and can be life-threatening. Haloperidol is not useful as a treatment for AIDS but may be a useful lead compound for the development of an antiviral pharmaceutical.

L4 ANSWER 32 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1990:420224 BIOSIS
DOCUMENT NUMBER: BA90:81025
TITLE: AN EDGE RELOCATION SEGMENTATION ALGORITHM.
AUTHOR(S): MACAULAY C; PALCIC B
CORPORATE SOURCE: CANCER IMAGING, BRITISH COLUMBIA CANCER RES. CENTRE, 601 WEST 10TH AVENUE, VANCOUVER, BRITISH COLUMBIA V5Z 1L3, CANADA.
SOURCE: ANAL QUANT CYTOL HISTOL, (1990) 12 (3), 165-171. CODEN: AQCHED. ISSN: 0884-6812.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB An automated procedure that refines the nuclear contour of a previously segmented nucleus is described. The algorithm makes use of intensity information, edge magnitude information and both object and edge connectivity information. This automated procedure generates a closed contour precisely along the edge of the nucleus. The procedure was tested on a **database** of 3,680 red-green-blue **images** of thionin-SO2 and orange II-stained cervical **cells** obtained from normal and dysplastic samples. When used in conjunction with a simple threshold selection algorithm and an artifact removal routine, this edge relocation algorithm resulted in the correct segmentation of over 98% of the nuclei. Only 63 (1.7%) of all nuclei were incorrectly segmented.

L4 ANSWER 33 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1989:242485 BIOSIS
DOCUMENT NUMBER: BA87:123550
TITLE: MICROINTERFEROMETRY OF THE MOVEMENT OF DRY MATTER IN FIBROBLASTS.
AUTHOR(S): BROWN A F; DUNN G A
CORPORATE SOURCE: MRC CELL BIOPHYSICS UNIT, KING'S COLL., 26-29 DRURY LANE,

LONDON WC2B 5RL, UK.
SOURCE: J CELL SCI, (1989) 92 (3), 379-390.
CODEN: JNCSAI. ISSN: 0021-9533.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB We desribe the use of interferometric microscopy coupled with a novel application of Senarmont compensation for detecting and quantifying the distribution of dry matter in cultured **cells**. In conjunction with video techniques and digtial **image** processing, a two-dimensional, calibrated map of the dry mass distribution in an isolated **cell** can be obtained and digitally recorded. We have called the technique digitally Recorded Interferometric Microscopy with Analyser Shift (DRIMAS). The method greatly facilitates the automatic recognition of **cells** by **computer**. Recorded time-lapse sequences can be used to establish a **database** of the growth and motility of specific **cells** in given experimental conditons. **Databases** of this type can be analysed to reveal the patterns of growth and locomotory behaviour of individual **cells**. We describe a systematic method of obtaining parameters of **cell** size, shape, spreading, intracellular motilty and translocation. Autocorrelations and cross-correlations between these parameters can be detected and quantified using time series analysis, revealing potential cause/effect relationsihps in the mechanisms of growth and motility. Besides characterizing the overall pattern of **cell** behaviour, these data can also yield information about the instantaneous pattern of intracellular motility. We describe the use of finite element analysis to reveal the dynamics of the intracellular transport of dry matter. This yields the pattern of the minimum flow of dry matter required to account for the changes in its distribution. Most of this flux is not associated with the movement of visible structures and possibly represents the transport of dissociated components of the cytoskeleton. In chick heart fibroblasts, surprisingly high velocities of nearly 2.0 .mu.m s-1 were detected during the period of increased motility following tail detachment. The total kinetic energy associated with the dry mass flux is a single parameter, which characterizes the instantaneous motility of the **cell**. We found that the kinetic energy of intracellular motilty can be several hundred times greater than the kinetic energy of translocation. Kinetic energy may prove to be a very informative single measure of intracellular motility for assessing the effects of malignant transformation, genetic manipulations, and other experimental treatments on the locomotory machinery of the **cell**.

L4 ANSWER 34 OF 34 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1988:506796 BIOSIS
DOCUMENT NUMBER: BA86:127480
TITLE: A TWO-DIMENSIONAL ELECTROPHORESIS STUDY OF PHOSPHORYLATION AND DEPHOSPHORYLATION OF CHROMAFFIN **CELL** PROTEINS IN RESPONSE TO A SECRETORY STIMULUS.
AUTHOR(S): GUTIERREZ L M; BALLESTA J J; HIDALGO M J; GANDIA L; GARCIA A G; REIG J A
CORPORATE SOURCE: DEP. NEUROQUIM., UNIV. ALICANTE, FAC. MED., 03690 ALICANTE, SPAIN.
SOURCE: J NEUROCHEM, (1988) 51 (4), 1023-1030.
CODEN: JONRA9. ISSN: 0022-3042.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Phoshorylated proteins of bovine chromaffin **cells**, radioactively labeled with [32P]orthophosphate, have been analyzed by two-dimensional polyacrylamide gel electrophoresis and autoradiography. Complex two-dimensional electrophoretograms were studied with the aid of **computer**-assisted **image** analysis (CAIA). A

database map of 32P-labeled proteins was constructed: .apprx. 500 polypeptides have been detected, numbered, and characterized according to the intensity of labeling, molecular weight, and isoelectric point. The **database** was constructed from **cells** kept in resting conditions or stimulated with 59 mM K+ in 2.5 mM Ca2+ or in 0 Ca2+ solution. These manipulations caused statistically significant changes in the degree of phosphorylation of 20 proteins; they were classified as Ca2+-dependent substrates for the phosphorylation or dephosphorylation processes. These changes were also shown in **cells** stimulated in the presence of the Ca2+ channel activator Bay K 8644. New proteins that show as much as a fivefold increase in their phosphorylation state during **cell** stimulation have been located with this methodology, as well as many others that had not previously been detected with conventional methods. These experiments provide the first CAIA **database** on chromaffin **cell** phosphoproteins; the map constructed with these data will allow the location of specific phosphoproteins and serve as a reference for future ongoing studies. The **database** will continue to grow to identify more proteins and to facilitate the comparison of complex patterns obtained in different laboratories for normal and transformed pheochromocytoma PC12 **cells**.

=> d his

(FILE 'HOME' ENTERED AT 07:51:42 ON 23 AUG 2000)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, SCISEARCH, BIOTECHDS' ENTERED AT 07:51:48 ON 23 AUG 2000

L1 2888 S HIGH()THROUGHPUT()SCREEN?
L2 14 S L1 AND COMPUTER AND DATABASE
L3 12 DUP REM L2 (2 DUPLICATES REMOVED)

=> d ibib abs l3 1-12

L3 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:250165 CAPLUS
DOCUMENT NUMBER: 133:58320
TITLE: Compound acquisition strategies
AUTHOR(S): Dunbar, James B., Jr.
CORPORATE SOURCE: Parke Davis Pharmaceutical Research Division, Warner Lambert Company, Ann Arbor, MI, 48015, USA
SOURCE: Pac. Symp. Biocomput. 2000 (2000), 555-565. Editor(s): Altman, Russ B. World Scientific Publishing Co. Pte. Ltd.: Singapore, Singapore. CODEN: 68UQA8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Compd. acquisition has always been a very important component in the discovery and development of new biol. active entities. With the rapid advances in **high throughput screening** coupled with the ever-decreasing time requirements for the discovery phase, the no. and quality of compds. screened is of great importance. Some of the techniques and processes that can be used in compd. acquisition are discussed.
REFERENCE COUNT: 20
REFERENCE(S): (2) Brown, R; J Chem Inf Comput Sci 1996, V36, P572 CAPLUS
(3) Brown, R; J Chem Inf Comput Sci 1997, V37, P1 CAPLUS
(4) Cramer, R; J Chem Inf Comput Sci 1998, V38, P1010 CAPLUS
(5) Cramer, R; J Med Chem 1996, V39, P3060 CAPLUS
(9) Lipinski, C; Adv Drug Delivery Rev 1997, V23(1-3), P3 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
ACCESSION NUMBER: 2000:234747 CAPLUS
DOCUMENT NUMBER: 133:261
TITLE: Property distribution of drug-related chemical **databases**
AUTHOR(S): Oprea, Tudor I.
CORPORATE SOURCE: Medicinal Chemistry, Astra Hassle AB, Moelndal, S-431 83, Swed.
SOURCE: J. Comput.-Aided Mol. Des. (2000), 14(3), 251-264 CODEN: JCADEQ; ISSN: 0920-654X
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The process of compd. selection and prioritization is crucial for both combinatorial chem. (CBC) and **high throughput screening** (HTS). Compd. libraries have to be screened for unwanted chem. structures, as well as for unwanted chem. properties. Property extrema can be eliminated by using property filters, in accordance with their actual distribution. Property distribution was examd. in the following compd. **databases**: MACCS-II Drug Data Report (MDDR), Current Patents Fast-alert, Comprehensive Medicinal Chem., Physician Desk Ref., New Chem. Entities, and the Available Chem. Directory (ACD). The ACDF and MDDRF subsets were created by removing reactive functionalities from the ACD and MDDR **databases**, resp. The ACDF subset was further filtered by keeping only mols. with a "drug-like" score below 0.8. The following properties were examd.: mol. wt. (MW), the calcd. octanol/water partition coeff. (CLOGP), the no. of rotatable (RTB) and rigid bonds (RGB), the no. of rings (RNG), and the no. of hydrogen bond donors (HDO) and acceptors (HAC). Of these, MW and CLOGP follow a Gaussian distribution, whereas all other descriptors have an asym. (truncated Gaussian) distribution. Four out of five compds. in ACDF and MDDRF pass the "rule of 5" test, a probability scheme that ests. oral absorption proposed by Lipinski et al. Because property distributions of HDO, HAC, MW and CLOGP (used in the "rule of 5" test) do not differ significantly between these datasets, the "rule of 5" does not distinguish "drugs" from "nondrugs". Therefore, Pareto analyses were performed to examine skewed distributions in all compd. collections. Seventy percent of the "drug-like" compds. were found between the following limits: 0 .ltoreq. HDO .ltoreq. 2, 2 .ltoreq. HAC .ltoreq. 9, 2 .ltoreq. RTB .ltoreq. 8, and 1 .ltoreq. RNG .ltoreq. 4, resp. The no. of launched drugs in MDDR having 0 .ltoreq. HDO .ltoreq. 2 is 4.8 times higher than the no. of drugs having 3 .ltoreq. HDO .ltoreq. 5. Skewed distributions can be exploited to focus on the "drug-like space": 62.68% of ACDF ("nondrug-like") compds. have 0 .ltoreq. RNG .ltoreq. 2, and RGB .ltoreq. 17, while 28.88% of ACDF compds. have 3 .ltoreq. RNG .ltoreq. 13, and 18 .ltoreq. RGB .ltoreq. 56. By contrast, 61.22% of MDDRF compds. have RNG .gtoreq. 3, and RGB .gtoreq. 18, and only 24.73% of MDDRF compds. have 0 .ltoreq. RNG .ltoreq. 2 rings, and RGB .ltoreq. 17. The probability of identifying "drug-like" structures increases with mol. complexity.

REFERENCE COUNT: 34
REFERENCE(S): (7) Chan, O; Drug Discov Today 1996, V1, P461 CAPLUS
(17) Lipinski, C; Adv Drug Deliv Rev 1997, V23, P3 CAPLUS
(23) Oprea, T; Proc Natl Acad Sci USA 1997, V94, P2133 CAPLUS
(26) Rishton, G; Drug Discov Today 1997, V2, P382 CAPLUS
(28) Sadowski, J; J Med Chem 1998, V41, P3325 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 12 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 2000:458379 SCISEARCH
THE GENUINE ARTICLE: 324JV
TITLE: Target-based drug discovery for the development of novel antiinfectives
AUTHOR: Selzer P M; Brutsche S; Wiesner P; Schmid P; Mullner H (Reprint)
CORPORATE SOURCE: INTERVET INTERNATL GMBH, DEPT PHARMACEUT RES, BLDG H811, D-65926 FRANKFURT, GERMANY (Reprint); INTERVET INTERNATL GMBH, DEPT PHARMACEUT RES, D-65926 FRANKFURT, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: INTERNATIONAL JOURNAL OF MEDICAL MICROBIOLOGY, (MAY 2000)
Vol. 290, No. 2, pp. 191-201.
Publisher: URBAN & FISCHER VERLAG, BRANCH OFFICE JENA, P O

BOX 100537, D-07705 JENA, GERMANY.
ISSN: 1438-4221.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 68
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In the 20(th) century and especially during the last 50 years, antiinfectives have been increasingly used to control and prevent infectious diseases. Unfortunately the resistance of microorganisms to these pharmaceuticals has increased as well. At the same time the discovery process for novel antiinfectives, the so-called ''conventional'' screening approach, involves testing natural products or derivatives of known compounds in in vitro cultures. By now it is obvious that this screening approach did not meet the expectations to generate a sufficient number of novel drug candidates. Consequently, studies for selective antiinfectives with new modes of action, which are able to break resistance, are highly desirable for human and animal health. The enormous advance in sequencing technologies - leading ro a constantly growing number of known microbial genomes - together with the rapid development of **computer** power and bioinformatic software tools, now makes it possible to identify genes and gene products that are essential to the pathogenic organisms and are therefore considered to be novel targets for the development of new antiinfectives. When these potential targets have been validated by sophisticated laboratory methods, large diverse compound libraries can be tested in in vitro assays using **high-throughput screening**. This approach will most likely generate an increasing number of novel lead structures that will be specifically optimized by modern combinatorial chemistry and subsequently lead to new antiinfective candidates strengthening the armoury of weapons available to fight infectious diseases in humans and animals.

L3 ANSWER 4 OF 12 MEDLINE
ACCESSION NUMBER: 2000133577 MEDLINE
DOCUMENT NUMBER: 20133577
TITLE: Structure-based inhibitor design.
AUTHOR: Craig S P 3rd; Eakin A E
CORPORATE SOURCE: Laboratory of Molecular Parasitology & Drug Design, University of North Carolina School of Pharmacy, Chapel Hill 27599-7360, USA.
SOURCE: VITAMINS AND HORMONES, (2000) 58 149-69. Ref: 57
Journal code: XFE. ISSN: 0083-6729.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
ENTRY MONTH: 200005
ENTRY WEEK: 20000501

AB Time and costs associated with the discovery of new drugs have been significantly reduced by enzyme structure-based approaches to the discovery of new chemotherapeutic agents. However, fundamental components of the overall approach continue to rely on technologies which, by their nature, involve relatively random processes (i.e., combinatorial chemistry and **high-throughput screening**). Thus, the efficiency of the drug discovery process potentially could be further improved through better use of structural information. In this regard, three-dimensional structures of enzymes are now being solved at high resolution and/or in conformations that provide data that should be more useful for inhibitor design or discovery. Scientists are beginning to appreciate the importance of water as a possible competitor of inhibitors

for binding to target enzymes. New computational algorithms are improving the efficiency of identifying flexible inhibitors from among the large numbers of compounds in chemical **databases**. Also, tools of molecular genetics together with structures of target enzymes are likely to be used more frequently in dealing with the development of resistance to novel chemotherapeutic agents. Instead of detailing success stories in structure-based drug discovery, the following article considers how future efforts to discover or design new drugs may increasingly rely on information about molecular targets and less on data acquired via approaches involving random methodologies.

L3 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:269098 CAPLUS
DOCUMENT NUMBER: 133:53086
TITLE: Combined molecular mechanical and continuum solvent approach (MM-PBSA/GBSA) to predict ligand binding
AUTHOR(S): Massova, Irina; Kollman, Peter A.
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of California at San Francisco, San Francisco, CA, 94143-0446, USA
SOURCE: Perspect. Drug Discovery Des. (2000), 18(Hydrophobicity and Solvation in Drug Design, Pt. II), 113-135
CODEN: PDDDEC; ISSN: 0928-2866
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Significant progress has been achieved in computational methods to treat solvent effects in recent years. Among various techniques, the continuum solvent approach appears to be practically promising because it can be used to calc. reliable interaction and solvation energies in complex systems. A computational scanning mutagenesis method, one of such new approaches, has been recently developed. It combines the mol. mech. and continuum solvent approaches and allows one to identify the "hot spots" in binding interfaces from a single trajectory of a wild type complex. Such techniques can be also used as a tool to optimize the interacting species for the binding, or as a ranking procedure in **high throughput screening**.
REFERENCE COUNT: 57
REFERENCE(S): (1) Bayly, C; J Phys Chem 1993, V97, P10269 CAPLUS
(2) Beroza, P; J Phys Chem 1996, V100, P20156 CAPLUS
(4) Bottger, A; J Mol Biol 1997, V269, P744 CAPLUS
(5) Brooks, B; J Comput Chem 1983, V4, P187 CAPLUS
(6) Chen, J; J Phys Chem 1994, V98, P11059 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:429200 CAPLUS
TITLE: From fields to pharmacophores: An historical perspective of explicit 3D molecular similarity calculations
AUTHOR(S): Good, Andrew C.
CORPORATE SOURCE: Bristol-Myers Squibb, Wallingford, CT, 06492-7660, USA
SOURCE: Internet J. Chem. (2000), 3, No pp. given, Article No. 9
CODEN: IJCHFJ
URL: http://www.ijc.com/article/2000v3/9/
PUBLISHER: Internet Journal of Chemistry
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Explicit three-dimensional (3D) mol. similarity calcns. may be defined as the quant. comparison of selected spatial mol. descriptors through the

application of a similarity equation (index). Such evaluations play a pivotal role in many areas of **computer**-aided mol. design (CAMD). In classical CAMD investigations they have typically been applied to the calcn. of optimum mol. superposition and as QSAR descriptors. More recently faster explicit mol. similarity evaluations have been advanced to allow their application in **database** searchers. With the advent of **high throughput screening** and combinatorial chem. the demand for faster calcns. has continued unabated. In answer to this a host of new alignment independent techniques have been developed to permit similarity calcns. over ever larger nos. of compds. The Richards group has made many seminal contributions in the creation of such methodol. This brief perspective summarizes these and other techniques in the context of current trends in the pharmaceutical industry. Recent advances are highlighted and potential future directions are discussed.

REFERENCE COUNT: 93

REFERENCE(S):
(1) Amat, L; Journal of Computational Chemistry 1998, V19, P1575 CAPLUS
(2) Amat, L; Journal of Computational Chemistry 1999, V20, P911 CAPLUS
(9) Badel, A; Journal of Molecular Graphics 1992, V10, P205 CAPLUS
(12) Blaney, F; Journal of Molecular Graphics 1993, V11, P98 CAPLUS
(13) Blaney, F; Journal of Molecular Graphics 1995, V13, P165 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 12 SCISEARCH COPYRIGHT 2000 ISI (R)

ACCESSION NUMBER: 2000:422652 SCISEARCH
THE GENUINE ARTICLE: 319JM

TITLE: From fields to pharmacophores: An historical perspective of explicit 3D molecular similarity calculations

AUTHOR: Good A C (Reprint)
CORPORATE SOURCE: BRISTOL MYERS SQUIBB CO, 5 RES PKWY, WALLINGFORD, CT 06492
(Reprint)
COUNTRY OF AUTHOR: USA

SOURCE: INTERNET JOURNAL OF CHEMISTRY, (3 MAY 2000) Vol. 3, No. 9-11, Sp. iss. SI, pp. U3-U21.
Publisher: INTERNET JOURNAL OF CHEMISTRY, C/O STEVEN M BACHRACH, NORTHERN ILLINOIS UNIV, DEPT CHEMISTRY, DE KALB, IL 60115.
ISSN: 1099-8292.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 93

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Explicit three-dimensional (3D) molecular similarity calculations may be defined as the quantitative comparison of selected spatial molecular descriptors through the application of a similarity equation (index). Such evaluations play a pivotal role in many areas of **computer**-aided molecular design (CAMD). In classical CAMD investigations they have typically been applied to the calculation of optimum molecular superposition and as QSAR descriptors. More recently faster explicit molecular similarity evaluations have been advanced to allow their application in **database** searches. With the advent of **high throughput screening** and combinatorial chemistry the demand for faster calculations has continued unabated. In

answer to this a host of new alignment independent techniques have been developed to permit similarity calculations over ever larger numbers of compounds. The [redacted]chards group has made many semi[redacted]l contributions in the creation of su[redacted]methodology. This brief perspec[redacted]ve summarizes these and other techniques in the context of current trends in the pharmaceutical industry. Recent advances are highlighted and potential future directions are discussed.

L3 ANSWER 8 OF 12 MEDLINE
ACCESSION NUMBER: 1999309316 MEDLINE
DOCUMENT NUMBER: 99309316
TITLE: Binary QSAR: a new method for the determination of quantitative structure activity relationships.
AUTHOR: Labute P
CORPORATE SOURCE: Chemical Computing Group Inc., Montreal, Quebec, Canada.
SOURCE: PACIFIC SYMPOSIUM ON BIOCOMPUTING, (1999) 444-55. Journal code: CWQ.
PUB. COUNTRY: Singapore
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY WEEK: 19991002
AB A new method (particularly suited to the analysis of **High Throughput Screening** data) is presented for the determination of quantitative structure activity relationships. The method, termed "Binary QSAR," accepts binary activity measurements (e.g., pass/fail or active/inactive) and molecular descriptor vectors as input. A
Bayesian inference technique is used to predict whether or not a new compound will be active or inactive. Experiments were conducted on a data set of 1947 molecules. The results show that the method exhibits high accuracy and is robust to measurement errors.

L3 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 2
ACCESSION NUMBER: 2000:15524 BIOSIS
DOCUMENT NUMBER: PREV200000015524
TITLE: Efficacy and selectivity in flexible **database** docking.
AUTHOR(S): Knegtel, Ronald M. A. (1); Wagener, Markus
CORPORATE SOURCE: (1) Vertex Pharmaceuticals (Europe) Ltd., 88 Milton Park, Milton, Abingdon, Oxon, OX14 4RY UK
SOURCE: Proteins, (Nov. 15, 1999) Vol. 37, No. 3, pp. 334-345. ISSN: 0887-3585.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Flexible **database** docking with DOCK 4.0 has been evaluated for its ability to retrieve biologically active molecules from a **database** of approximately 1,000 compounds with known activities against thrombin and the progesterone receptor. The retrieval of known actives and chemically similar but inactive molecules was monitored as a function of conformational and orientational sampling. The largest enrichment of actives among the 10% highest ranking molecules is obtained when only five conformations are used to seed the next round of ligand reconstruction and limited sampling is applied to place the base fragment in the binding site. The performance of energy and chemical scoring, as implemented in DOCK 4.0, was found to depend on the protein used for docking. For the progesterone receptor, energy scoring yields the largest enrichments (64%) in terms of actives retrieved among the 10% top scoring molecules, while chemical scoring performs best for thrombin (94%). With the exception of the application of energy scoring to the progesterone receptor, both energy-based scoring schemes applied in this study do not discriminate well between true actives and chemically similar but inactive
compounds. In conclusion, flexible docking is able to effectively

prioritize **high-throughput screening databases**, using less conformational sampling than normally required for appropriate reconstruction of protein-ligand complexes. The more subtle discrimination between chemically similar classes of active and inactive compounds remains, however, problematic.

L3 ANSWER 10 OF 12 MEDLINE
ACCESSION NUMBER: 1999186275 MEDLINE
DOCUMENT NUMBER: 99186275
TITLE: Design of libraries to explore receptor sites.
AUTHOR: Murray C M; Cato S J
CORPORATE SOURCE: Chemical Design Ltd., Cromwell Park, Chipping Norton, UK.
SOURCE: JOURNAL OF CHEMICAL INFORMATION AND COMPUTER SCIENCES, (1999 Jan-Feb) 39 (1) 46-50.
Journal code: HNT. ISSN: 0095-2338.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY WEEK: 19990504
AB Despite rapid progress in both combinatorial chemistry and **high-throughput screening**, the number of molecules that could potentially be made and tested for biological activity still far exceeds the capacity for synthesis or screening. Consequently, it is potentially valuable to select and synthesize sublibraries that contain rationally selected subsets. When the structure of the protein receptor site is known, this may be used to impose restrictions of the selection on molecules. This paper describes a method for rapid analysis of large virtual libraries to select a subset that can exhibit at least one conformer which wil interact strongly with the receptor and fit within the receptor site.

L3 ANSWER 11 OF 12 MEDLINE
ACCESSION NUMBER: 1998374290 MEDLINE
DOCUMENT NUMBER: 98374290
TITLE: A **high throughput screen** to identify secreted and transmembrane proteins involved in Drosophila embryogenesis.
AUTHOR: Kopczynski C C; Noordermeer J N; Serano T L; Chen W Y; Pendleton J D; Lewis S; Goodman C S; Rubin G M
CORPORATE SOURCE: Department of Molecular and Cell Biology, Howard Hughes Medical Institute, University of California, Berkeley, CA 94720-3200, USA.
CONTRACT NUMBER: HG00750 (NHGRI)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Aug 18) 95 (17) 9973-8.
Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-AA140639; GENBANK-AA140640; GENBANK-AA140641; GENBANK-AA140642; GENBANK-AA140643; GENBANK-AA140644; GENBANK-AA140645; GENBANK-AA140646; GENBANK-AA140647; GENBANK-AA140648; GENBANK-AA140649; GENBANK-AA140650; GENBANK-AA140651; GENBANK-AA140652; GENBANK-AA140653; GENBANK-AA140654; GENBANK-AA140655; GENBANK-AA140656; GENBANK-AA140657; GENBANK-AA140658; GENBANK-AA140659; GENBANK-AA140660; GENBANK-AA140661; GENBANK-AA140662; GENBANK-AA140663; GENBANK-AA140664; GENBANK-AA140665; GENBANK-AA140665; GENBANK-AA140666; GENBANK-AA140667; +
ENTRY MONTH: 199811
AB Secreted and transmembrane proteins play an essential role in intercellular communication during the development of multicellular

organisms. Because only a small number of these genes have been characterized, we developed a screen for genes encoding extracellular proteins that are differentially expressed during Drosophila embryogenesis. Our approach utilizes a new method for screening large numbers of cDNAs by whole-embryo in situ hybridization. The cDNA library for the screen was prepared from rough endoplasmic reticulum-bound mRNA and is therefore enriched in clones encoding membrane and secreted proteins. To increase the prevalence of rare cDNAs in the library, the library was normalized using a method based on cDNA hybridization to genomic DNA-coated beads. In total, 2,518 individual cDNAs from the normalized library were screened by in situ hybridization, and 917 of these cDNAs represent genes differentially expressed during embryonic development. Sequence analysis of 1,001 cDNAs indicated that 811 represent genes not previously described in Drosophila. Expression pattern photographs and partial DNA sequences have been assembled in a **database** publicly available at the Berkeley Drosophila Genome Project website (). The identification of a large number of genes encoding proteins involved in cell-cell contact and signaling will advance our knowledge of the mechanisms by which multicellular organisms and their specialized organs develop.

L3 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:29746 CAPLUS
DOCUMENT NUMBER: 126:69585
TITLE: Flexible three-dimensional **database** searching for the identification of novel lead compounds
AUTHOR(S): Finn, P. W.; Snarey, M.
CORPORATE SOURCE: Pfizer Central Research, Kent, CT13 9NJ, UK
SOURCE: Bioact. Compd. Des. (1996), 67-76. Editor(s): Ford, Martyn G. Bios Scientific Publishers: Oxford, UK. CODEN: 63SXAI
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 8 refs. **High-throughput screening** of compd. libraries, most commonly the file of compds. in a corporate **database** built up over many years, has proven successful at identifying new leads for subsequent optimization by medicinal chem. In addn. to the phys. file of samples, most companies also maintain computerized versions of these files, contg. registry nos., structures and biol. activities. For many years, searches of these **computer** files have been performed in attempts to discover leads, but it is only recently, with the addn. of three-dimensional information to these **databases**, and the inclusion of mol. flexibility, that computational searching has come of age. The authors illustrate the use of three-dimensional flexible **database** searching with the identification of a novel structure with high affinity for the neurokinin receptor and the identification of novel structural elements contained in potent muscarinic antagonists. The use of **database** searching for lead finding will grow in the future, esp. as applied to "virtual **databases**".